

LISTING OF CLAIMS

1. *(currently amended)*: A method of treating a deficiency of a Hedgehog protein in the GI tract of a subject deficient in said protein and in need of such treatment, wherein the method comprises comprising providing a source of Hedgehog protein to the GI tract of the [[a]] subject suffering from the deficiency of a Hedgehog protein in the GI tract a composition that comprises a source of a Hedgehog protein.
2. *(currently amended)*: A method according to claim [[1]] 30, wherein the subject is at risk for, or suffers from cancer of the GI tract and said providing results in
 - (i) prevention of said cancer development, or
 - (ii) therapy of said cancer ~~the source of Hedgehog protein is provided to the GI tract of a subject suffering from the deficiency of a Hedgehog protein for the prophylaxis of carcinogenesis in the GI tract.~~
3. *(currently amended)*: A method according to claim 2, wherein the cancer is source of Hedgehog protein is provided for the prophylaxis of gastric or colon[[ic]] cancer.
4. *(currently amended)*: A method according to claim [[1]] 2, wherein the source of Hedgehog protein is provided to the GI tract of a subject suffering from the deficiency of a Hedgehog protein for the treatment of a cancer is a GI tract carcinoma and said providing results in therapy of said carcinoma.
5. *(currently amended)*: A method according to claim 4, wherein the GI tract carcinoma is a gastric or colon[[ic]] carcinoma cancer.
6. *(currently amended)*: A method according to ~~any one of claim~~[[s]] 1 [[- 5]], wherein the deficiency of the [[a]] Hedgehog protein is an acquired deficiency of a Hedgehog protein.
7. *(currently amended)*: A method according to claim 30 ~~any one of claims 1—5~~, wherein the subject suffering from the deficiency of a Hedgehog protein in the GI tract is a subject having been diagnosed with has familial adenomatous polyposis coli (FAP).

8. *(currently amended)*: A method according to claim 7, wherein the ~~source of~~ Hedgehog protein, homologue or variant, nucleic acid expression vector, bacterial delivery vehicle, animal cell or inducing or upregulating agent, is administered in an amount effective to prevent or reverse GI tract tumorigenesis in the FAP subject ~~having been diagnosed with FAP~~.

9. *(currently amended)*: A method according to claim 7, wherein the ~~source of~~ Hedgehog protein, homologue or variant, nucleic acid expression vector, bacterial delivery vehicle, animal cell or inducing or upregulating agent, is administered in an amount effective to prevent or reverse colonic adenomatous polyps, ~~and~~ invasive adenocarcinomas, small intestinal adenomas and cancers, and desmoid tumors.

10. *(currently amended)*: A method according to claim 30 ~~any one of claims 1—9~~, wherein the source of Hedgehog protein comprises is a pharmaceutical composition comprising a ~~the~~ Hedgehog protein, homologue or variant in a pharmaceutical composition.

11. *(original)*: A method according to claim 10, wherein the pharmaceutical composition is suitable for oral administration.

12. *(currently amended)*: A method according to claim 30 ~~any one of claims 1—9~~, wherein the source of the Hedgehog protein comprises said ~~is a pharmaceutical composition comprising gene therapy~~ nucleic acid vector ~~wherein the vector comprises a nucleotide sequence encoding a~~ Hedgehog protein in a pharmaceutical composition.

13. *(currently amended)*: A method according to claim 30 ~~any one of claims 1—9~~, wherein the source of Hedgehog protein comprises said ~~is a pharmaceutical composition comprising an enteric bacterium wherein the bacterium comprises a nucleotide sequence encoding a Hedgehog protein, and whereby the nucleotide sequence confers to the bacterium the ability to secrete the Hedgehog~~ protein.

CLAIMS 14-24: CANCELLED

25. *(currently amended)*: A method for determining whether diagnosing the status of a subject is at risk for developing a ~~with respect to~~ GI tract tumorigenesis, ~~the method comprising measuring~~ determining the level of a Hedgehog protein or a Hedgehog mRNA in a GI tract tissue sample~~[[s]]~~ obtained from the subject.

26. *(currently amended)*: A method according to claim 25, wherein the tissue sample is a ~~sample of~~ gastric, esophageal~~[[ic]]~~ or colon~~[[ic]]~~ tissue~~[[s]]~~.

27. *(currently amended)*: A method for diagnosing (i) the susceptibility of a subject to develop ~~for development of~~, or (ii) the presence in a subject of, ectopic gastric tissue ~~in a subject, whereby~~ the method comprising comprises determining the ~~mRNA or protein~~ level of Hedgehog, BMP2 or BMP4 mRNA and/or protein in a tissue sample from the subject.

28. *(currently amended)*: A therapeutic composition ~~gene therapy vector~~ comprising a nucleotide sequence encoding a Hedgehog protein which composition is in the form of.

(a) a nucleic acid expression vector; or

(b) an enteric bacterium comprising the nucleotide sequence which bacterium is capable of secreting the Hedgehog protein when colonizing the GI system of a subject.

29. *(currently amended)*: The therapeutic composition of claim 28 which is said ~~An~~ enteric bacterium ~~comprising a nucleotide sequence encoding a Hedgehog protein, whereby the nucleotide sequence confers to the bacterium the ability to secrete the Hedgehog protein.~~

30. *(new)* The method of claim 1 wherein said source of Hedgehog protein is:

(a) a Hedgehog protein or an active homologue or variant thereof;

(b) a nucleic acid expression vector comprising a nucleotide sequence that encodes said protein, homologue or variant;

(c) an enteric bacterium capable of colonizing a part of the GI tract which is transformed with said encoding nucleotide sequence and expresses and secretes said Hedgehog protein, homologue or variant;

(d) an animal cell that expresses and secretes said Hedgehog protein, homologue or variant; or

(e) a molecule or agent that induces or upregulates expression of Hedgehog protein in said subject.

31. *(new)*: The method of claim 30 wherein said Hedgehog protein is Shh or Ihh and said homologue or variant is a homologue or variant of Shh or Ihh.

32. *(new)*: A method for preventing the development or treating a disease or condition characterized by the presence or growth of a Hedgehog protein-expressing ectopic gastric tissue in a subject, comprising providing to the subject or to the site of said ectopic tissue an effective amount of a substance that reduces the functional level or activity of the Hedgehog protein.

33. *(new)*: A method according to claim 32, wherein said substance is an antibody specific for said Hedgehog protein or an antisense nucleic acid at least part of which is complementary to at least a functional part of a Hedgehog mRNA that encodes a Hedgehog protein selected from the group consisting of human Desert Hedgehog protein SEQ ID NO:1, human Indian Hedgehog protein SEQ ID NO:2, and human Sonic Hedgehog protein SEQ ID NO:3.